

EBM conference

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Clinical scenario

- 73 year-old woman
- Diffuse large B-cell lymphoma with multiple lymphadenopathies, Stage IVBE
- chemotherapy started from 19/11/2008
 - *Cyclophosphamide*
 - *Doxorubicin*
 - *Vincristine*
 - *Prednisolone*
- Prevention of tumour lysis syndrome

Clinical scenario (cont'd)

- Pre-Chemotheapy
 - 8/11 LDH: 369 IU/L ; Uric acid 2.8mg/dL
 - 13/11 LDH: 430 IU/L ; Uric acid 5.5mg/dL
- Post-Chemotheapy
 - 20/11 LDH: 607 IU/L; Uric acid 7.4mg/dL

Clinical Problem

- What shall we chose to do in order to prevent her suffers from tumour lysis syndrome?

Clinical Problem (PICO)

P	73 year-old woman Diffuse large B-cell lymphoma with multiple lymphadenopathies undergo chemotherapy
I	<i>Rasburicase or allopurinol</i>
C	fluid hydration only
O	Better pretreatment agent for tumour lysis syndrome on prognosis and economical consideration

Search

- Key words
 - Tumour lysis syndrome
 - Prevention
- Database
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 - National Library for health

Results

The screenshot shows a web browser displaying the UpToDate website. The address bar shows the URL: http://www.uptodate.com/online/content/topic.do?topicKey=chemagen/4930&selectedTitle=1~75&source=search_result. The page title is "Tumor lysis syndrome".

TOPIC OUTLINE

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- PATHOGENESIS
 - Hyperuricemia
 - Hyperphosphatemia
 - Xanthinuria
- CLINICAL MANIFESTATIONS
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 - Hematologic malignancies
 - Solid tumors
 - Spontaneous TLS
 - Risk stratification
 - Risk stratification in AML
- PREVENTION
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 - Urinary alkalization
 - Allopurinol
 - Dosage and administration
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 - Dosing and administration
 - Contraindications and restrictions
 - Monitoring guidelines
- TREATMENT OF ESTABLISHED TLS
 - Electrolyte abnormalities
 - Indications for dialysis
- SUMMARY AND

Tumor lysis syndrome

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Last literature review version 16.3: 十月 2008 | **This topic last updated:** 九月 2, 2008 [\(More\)](#)

INTRODUCTION — Tumor lysis syndrome (TLS) is an oncologic emergency that is caused by massive tumor cell lysis with the release of large amounts of potassium, phosphate, and nucleic acids into the systemic circulation. Catabolism of the nucleic acids to uric acid leads to hyperuricemia, and a marked increase in uric acid excretion can result in the precipitation of uric acid in the renal tubules and acute renal failure. Hyperphosphatemia with calcium phosphate deposition in the renal tubules can also cause renal failure.

TLS most often occurs after the initiation of cytotoxic therapy in patients with high-grade lymphomas (particularly the Burkitt subtype) and acute lymphoblastic leukemia. However, TLS can occur spontaneously and with other tumor types that have a high proliferative rate, large tumor burden, or high sensitivity to cytotoxic therapy.

The best management of TLS is prevention. The preventive regimen consists of aggressive intravenous hydration, and the administration of the hypouricemic agents [rasburicase](#) (recombinant urate oxidase) or [allopurinol](#). (See "Prevention" below).

The definition, classification, pathogenesis, etiology, clinical presentation, prevention, and treatment of TLS will be reviewed here. Issues related to treatment of the particular malignancies that are associated with TLS are discussed separately. (See "[Treatment of Burkitt leukemia/lymphoma](#)", section on Tumor lysis syndrome, and see "[Treatment of adult T-cell lymphoma/leukemia](#)", and see "[Overview of the treatment of acute lymphoblastic leukemia in children](#)", section on Tumor lysis syndrome, and see "[Complications of acute myeloid leukemia](#)", section on Tumor lysis syndrome).

DEFINITION AND CLASSIFICATION — Although there is a general consensus that TLS represents a set of metabolic complications that arise from treatment of a rapidly proliferating and drug-sensitive neoplasm, there have been relatively few attempts to specifically define the syndrome [1,2]. The 1993 Hande-Garrow classification system distinguished between laboratory versus clinical TLS in the four days following treatment, but did not take into account patients who already had abnormal laboratory values prior to treatment or those who developed metabolic abnormalities at a later time point [3].

Cairo-Bishop definition — The Cairo-Bishop definition, proposed in 2004, modified the Hande-Garrow classification by providing specific laboratory criteria for the diagnosis of TLS both at presentation and within seven days of treatment [2]. It also incorporated a grading system to help delineate the degree of severity of TLS.

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Recommendations

- For all patients at high or intermediate risk of TLS
 - recommend aggressive fluid hydration (2 to 3 L/m² daily) to achieve a urine output of at least 80 to 100 mL/m² per hour (**Grade 1A**).
 - If there is no evidence of acute obstructive uropathy and/or hypovolemia
 - diuretics may be used to maintain the urine output, if necessary.

Recommendations (cont'd)

- For the initial management of both adult and pediatric patients at **high risk** for TLS,
 - recommend rasburicase rather than allopurinol (**Grade 1A**).

Patient stratification by risk for tumor lysis syndrome

Patient stratification by risk for tumor lysis syndrome

Type of cancer	Risk		
	High	Intermediate	Low
NHL	Burkitt's, lymphoblastic, B-ALL	DLBCL	Indolent NHL
ALL	WBC \geq 100,000/microL	WBC 50,000-100,000/microL	WBC \leq 50,000/microL
AML	WBC \geq 50,000/microL, monoblastic	WBC 10,000-50,000/microL	WBC \leq 10,000/microL
CLL		WBC 10,000-100,000/microL treated with fludarabine	WBC \leq 10,000/microL
Other hematologic malignancies (including CML and multiple myeloma) and solid tumors		Rapid proliferation with expected rapid response to therapy	Remainder of patients

NHL: non-Hodgkin's lymphoma; B-ALL: Burkitt's acute lymphoblastic leukemia; DLBCL: diffuse large B-cell lymphoma; ALL: acute lymphoblastic leukemia; AML: acute myeloid leukemia; CLL: chronic lymphocytic leukemia; Tx: treatment; CML: chronic myeloid leukemia.

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Level of evidences

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

Level	Therapy/Prevention, Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval‡)	Individual inception cohort study with ≥ 80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absolute better-value or worse-value analyses ††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR† or validated on split-sample§§§ only	Exploratory** cohort study with good††† reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Grades of Recommendation

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A	consistent level 1 studies
B	consistent level 2 or 3 studies or extrapolations from level 1 studies
C	level 4 studies or extrapolations from level 2 or 3 studies
D	level 5 evidence or troublingly inconsistent or inconclusive studies of any level

"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.

Critical Appraisal

- Will the results help me in caring for my patient?
(External Validity/Applicability)
 - yes
- Is my patient so different to those in the study that the results cannot apply?
 - no
- Is the treatment feasible in my setting?
 - yes
- Will the potential benefits of treatment outweigh the potential harms of treatment for my patient?
 - no

Reviews

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Title: Rasburicase in the prevention and treatment of tumour lysis syndrome.

Citation: Intensive & critical care nursing : the official journal of the British Association of Critical Care Nurses, February 2008, vol./is. 24/1(59-62), 0964-3397

Author(s): Mayne N,Keady S,Thacker M

Abstract: Tumour lysis syndrome (TLS) can be a life threatening complication of cancer therapy where cells undergo overwhelming lysis. The result is a pattern of metabolic abnormalities leading to acute renal failure and possible coagulopathy. Prophylactic pharmaceutical interventions can prevent this syndrome in almost all patients reducing possible admission to the intensive care unit. This article reviews the clinical efficacy, side effect profile, dosing and administration of rasburicase, an intravenous recombinant urate oxidase used in patients at risk of Tumour lysis syndrome due to a high tumour burden or where treatment is required. Rasburicase is an expensive but effective treatment option in the prevention and treatment of tumour lysis syndrome.

Language: ENG

Publication type: Journal Article

Subject Heading (s): [Allopurinol/therapeutic use](#)
[Gout Suppressants/*therapeutic use](#)
[Humans](#)
[Intensive Care Units](#)
[Tumor Lysis Syndrome/*prevention & control](#)
[Urate Oxidase/*therapeutic use](#)

Source: MEDLINE from PubMed

Results

- In lower risk patient groups
 - allopurinol remains drug of choice as its safety and efficacy is well established and is a fraction of the price.
- Acute T and B cell lymphoblastic leukaemia and non-Hodgkin's lymphoma (NHL) i.e. Burkitt's and lymphoblastic lymphomas (high risk)
 - likely to require rasburicase due to its superior efficacy and route of administration.
 - Although allopurinol does have an IV form
 - this is unlicensed, hard to obtain and less effective.

Recommendations

- This article reviews
 - clinical efficacy
 - side effect profile
 - dosing and administration of *rasburicase*
- *Rasburicase* is an **expensive but effective treatment** option in the prevention and treatment of tumour lysis syndrome.

Level of evidences

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"Extrapolations" are where data is used in a situation which has potentially clinically important differences than the original study situation.

Critical Appraisal

- Is the economic evaluation likely to be usable?
 - yes
- How were costs and consequences assessed and compared?
 - yes
- Will the results help in purchasing services for local people?
 - yes

Conclusion

- Our patient is in the **intermediated risk**
- As concern on the medical costs and the availability in our hospital, we will apply allopurinol first
- Regular follow-check of LDH and uric acid levels
 - administration of *rasburicase* if uric acid levels are ≥ 8 mg/dL



Thanks for your attention